

## NOVEL COMPOUNDS, THEIR PREPARATION AND USE

### CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority under 35 U.S.C. 119 of Danish application no. PA  
5 2002 01629 filed October 28, 2002 and U.S. application no. 60/423,644 filed November 4,  
2002, the contents of each of which are fully incorporated herein by reference.

### FIELD OF THE INVENTION

The present invention relates to novel compounds, to the use of these compounds  
as pharmaceutical compositions, to pharmaceutical compositions comprising the compounds  
10 and to a method of treatment employing these compounds and compositions. More specifi-  
cally, the compounds of the invention can be utilised in the treatment and/or prevention of  
conditions mediated by the Peroxisome Proliferator-Activated Receptors (PPAR), in particu-  
lar the PPAR $\delta$  subtype.

### BACKGROUND OF THE INVENTION

15 Coronary artery disease (CAD) is the major cause of death in Type 2 diabetic and  
metabolic syndrome patients (i.e. patients that fall within the 'deadly quartet' category of im-  
paired glucose tolerance, insulin resistance, hypertriglyceridaemia and/or obesity).

The hypolipidaemic fibrates and antidiabetic thiazolidinediones separately display  
moderately effective triglyceride-lowering activities although they are neither potent nor effi-  
20 cacious enough to be a single therapy of choice for the dyslipidaemia often observed in Type  
2 diabetic or metabolic syndrome patients. The thiazolidinediones also potently lower circu-  
lating glucose levels of Type 2 diabetic animal models and humans. However, the fibrate  
class of compounds are without beneficial effects on glycaemia. Studies on the molecular  
actions of these compounds indicate that thiazolidinediones and fibrates exert their action by  
25 activating distinct transcription factors of the peroxisome proliferator activated receptor  
(PPAR) family, resulting in increased and decreased expression of specific enzymes and  
apolipoproteins respectively, both key-players in regulation of plasma triglyceride content.  
Fibrates, on the one hand, are PPAR $\alpha$  activators, acting primarily in the liver. Thiazolidin-  
ediones, on the other hand, are high affinity ligands for PPAR $\gamma$  acting primarily on adipose  
30 tissue.

Adipose tissue plays a central role in lipid homeostasis and the maintenance of  
energy balance in vertebrates. Adipocytes store energy in the form of triglycerides during  
periods of nutritional affluence and release it in the form of free fatty acids at times of